REMARKS

Status of the Claims

Claims 24-56 are in the application.

Claims 24-56 were rejected.

Claims 27-29, 37-39, 47, and 52 have been amended Upon entry of this amendment, claims 24-56 will be pending.

Summary of the Amendment

Claims 27 and 37 have been amended to be rewritten in independent form. Claims 28, 29 and 47 have been amended to depend upon claim 27. Claims 38, 39, and 52 have been amended to depend upon claim 37. No new matter has been added.

Claim Rejection Under 35 U.S.C. § 112, first paragraph

Claims 24-56 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabled for the full scope of the claims. The Office admits that the specification does enable methods for treating individuals who have metastasized colorectal cancer or who have been identified as being susceptible to metastasized colorectal cancer comprising administering a therapeutically effective or prophylactically effective amount of a viral vector comprising a nucleic acid sequence encoding amino acids 24-454 as set forth in SEQ ID NO: 2. The Office alleges that the specification does not enable methods for treating individuals who have metastasized colorectal cancer or who have been identified as being susceptible to metastasized colorectal cancer comprising administering a therapeutically effective or prophylactically effective amount of "just any composition comprising a nucleic acid molecule that encodes just any epitope of just any human guanylyl cyclase C protein." (Office Action, page 3). The Office alleges that it would require undue experimentation to practice the claimed methods. Applicant respectfully disagrees.

It is well settled that working examples are not absolutely required. Moreover, the specification does refer to the claimed subject matter, *i.e.* human guanylyl cyclase C and the

extracellular domain of human guanylyl cyclase C. In view of the specification and the previously filed declaration executed by inventor Scott A. Waldman the pending claims are enabled. Furthermore, the Office has failed to put forward any reasonable evidence in view of the specification and the declaration that raises doubt as to the enablement of the pending claims. As previously stated, the disclosure and the data provided in the Waldman declaration make clear that the claimed invention is operable *in vivo*. The evidence is sufficient to support a finding that one skilled in the art would conclude that the claimed invention is enabled. In particular, the data in Figure 3 of the Snook reference (previously filed by Applicant on May 2, 2008 as Exhibit A) show that immunization protected against lung metastasis in animals challenged with GCC-expressing colorectal cancer cells. The data in the Snook manuscript (previously filed by Applicant on May 2, 2008 as Exhibit B) show immunization with GCC-expressing viral vectors opposed the formation of nascent metastases to liver and extended the median survival of mice with established lung metastases following therapeutic immunization. Based upon these experiments and accompanying data and the specification one skilled in the art would conclude that the claims are enabled.

The Office cites two references (Verma et al, Nature, 1997, 389:239-242) and Amalfitano (Current Gene Therapy 2002, 2: 111-133) to suggest that the pending claims are not enabled. However, the evidence put forward by the Office does not raise doubt as to the enablement of the pending claims. The pending claims, specification, and declaration cannot be viewed in separately but must be taken as a whole. Taken as a whole the claims are enabled. The declaration and specification demonstrates that introduction of a nucleic acid molecule that encodes an extracellular domain of human guanylyl cyclase C protein (Claims 27 and 37) is enabled. Therefore, one of skill in the art would also understand that a nucleic acid encoding a protein that comprises or consists of human guanylyl cyclase C protein (claims 28, 29, 39, and 40) are also enabled. The Office's use of articles unrelated to the present specification and pending claims do not give rise to doubt or that it would require undue experimentation to practice the claimed methods.

The Verma and Amalfitano references are not related because they refer to gene therapy where the desired result is persistent gene expression over a long period of time. In contrast, the present claims are not directed to gene therapy where one needs persistent gene expression. The pending claims are directed to methods of treatment where the vaccine expresses the protein as described in the claims, which is in contrast to the gene therapy described in the Verma and the Amalfitano references.

As the M.P.E.P. states, "the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention." (Section 2164.04). Although the Examiner has cited two references to question the enablement of the pending claims because they are directed to gene therapy (i.e. persistent expression of a gene) rather than the methods of treatment as recited in the pending claims the references do not establish a reasonable basis to question the enablement of the pending claims.

For example, the Amalfitano reference discuss "human gene therapy" and defines the primary objective as the ability to "deliver a functional gene to tissues where the respective gene activity is missing or defective." (p. 111, left column, first paragraph). Similarly, in the Verma reference it discusses "putting corrective genetic material into cells" to "alleviate the symptoms of disease" and states that problems exist due to "lack of sustained expression." (Verma, Abstract, and first full paragraph, p. 239). These statements have nothing to do with the pending claims, which do not require persistent expression or replacing a defective or missing gene. Therefore, the Office has failed to establish a reasonable basis to question the enablement of the pending claims.

Even if the Office has established its burden, Applicants have sufficient evidence to rebut an allegation of non-enablement. As previously stated here and in the response filed May 2, 2008 the declaration executed by inventor Scott Waldman along with the specification demonstrates that the claims are enabled. The broadest claims are enabled because the data demonstrate that a vaccine that encodes a protein comprising at least one epitope of human guanylyl cyclase C protein is enabled (Claims 24 and 25). The data further demonstrates that a protein that encodes the extracellular domain or those that comprises an epitope of amino acids

24-454 of SEQ ID NO: 2 or a protein that comprises SEQ ID NO:2 is also enabled because the construct that was used comprised an epitope comprising those residues or epitopes thereof. Thus, the skilled artisan would believe that the pending claims are enabled taking into account the specification and the declaration of Scott Waldman.

Applicant notes that the Office's rejection is particular to the independent claims 24 and 25 but is not relevant to claims 27 and 37 (now independent) which are directed to the extracellular domain of the protein. As discussed in detail above, the claims directed to the extracellular domain or to the specific regions (amino acid residues 24-454) are enabled and the Office has failed to raise a reasonable doubt as to why they are not enabled in view of the Waldman declaration. Applicant respectfully requests that even if the rejection is maintained over claims 24 and 25, that claims 27 and 37 and the claims that depend upon the same are enabled for the reasons stated above.

Therefore, because the Office has failed to establish a reasonable basis to question the enablement of the claims because the cited references are not relevant to the pending claims, the pending claims are enabled. Furthermore, as discussed above, even if the Office had established a reasonable basis, the basis has been rebutted in view of the specification and the Waldman declaration. Accordingly, Applicant requests that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

Conclusion

Claims 24-56 are in condition for allowance. A notice of allowance is earnestly solicited. Applicants invite the Examiner to contact the undersigned at 610.640.7820 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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